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MORPHOFUNCTIONAL CORRELATIONS IN THE EXPERIMENTAL STUDY OF
MYOCARDIOPATHIES UNDER THE STRESS OF FORCED RESTRAINT.
NOTE II. THE INFLUENCE OF ADRENAL IMBALANCE

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E. Dughir

(NASA-TM-76138) MORPHOFUNCTIONAL
CORRELATIONS IN THE EXPERIMENTAL STUDY OF
MYOCARDIOPATHIES UNDER THE STRESS OF FORCED
RESTRAINT. NOTE 2: THE INFLUENCE OF
ADRENAL (National Aeronautics and Space

N80-28040

Unclas

G3/52 27953

Translation of "Corelatii Morfofunctionale in Studiul
Experimental Al Miocardopatiilor din Timpul Stressului
Prin Imobilizare Fortata," Revue Medico-Chirurgicale (Iasi)
(Romania), No. 1, 1978, pp 87-91



NATIONAL AERONAUTICS AND SPACE ADMINISTRATION
WASHINGTON, D.C. 20546

MAY 1980

STANDARD TITLE PAGE

1. Report No. NASA TM-76138		2. Government Accession No.		3. Recipient's Catalog No.	
4. Title and Subtitle MORPHOFUNCTIONAL CORRELATIONS IN THE EXPERIMENTAL STUDY OF MYOCARDIO- PATHIES UNDER THE STRESS OF FORCED RESTRAINT NOTE II. THE INFLUENCE OF ADRENAL IMBALANCE				5. Report Date May 1980	
				6. Performing Organization Code	
7. Author(s) M. Dinu, S. Dolinescu, A. Sneer, M. Mihaila and E. Dughir				8. Performing Organization Report No. NASW- 3199	
				10. Work Unit No.	
9. Performing Organization Name and Address Leo Kanner Associates Redwood City, CA 94063				11. Contract or Grant No.	
				13. Type of Report and Period Covered translation	
12. Sponsoring Agency Name and Address National Aeronautics and Space Adminis- tration, Washington, D.C. 20546				14. Sponsoring Agency Code	
15. Supplementary Notes Translation of "Corelatii Morfofunctionale in Studiul Experimental Al Miocardiopatiilor din Timpul Stresului Prin Imobilizare Fortata," Revue Medico-Chirurgicale (Iasi) (Romania), No. 1, 1978, pp 87-91					
16. Abstract The experimental study carried out showed that in rats with adrenal imbalance, fasting and restraint produced the same biochemical alterations as in the controls. The morphologic alterations, as well as their electric expression, were more varied and evident in the animals with adrenal imbalance. Persistence of the microscopic and electro- cardiographic alterations after 72 hours restraint in the animals subjected to unilateral adrenalectomy suggests chronic evolution of the myocardial lesions. This proves the necessity of intact adrenals for a good adaptability to stress.					
17. Key Words (Selected by Author(s))			18. Distribution Statement Unclassified-Unlimited		
19. Security Classif. (of this report) Unclassified		20. Security Classif. (of this page) Unclassified		21. No. of Pages 12	
				22. Price	

MORPHOFUNCTIONAL CORRELATIONS IN THE EXPERIMENTAL STUDY OF
MYOCARDIOPATHIES UNDER THE STRESS OF FORCED RESTRAINT.

NOTE II. THE INFLUENCE OF ADRENAL IMBALANCE

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In our previous studies [4, 12] we have pointed out, as did /87*
other authors [1, 10, 11], the role of stress states in the appearance of
myocardiopathies.

Many observations revealed that under adaptive stress conditions
the demand for corticoids increases considerably [1, 2, 5, 6, 7, 8, 11].
On the basis of these data we believed it necessary to follow up in
a new investigation the effect of restraint on the function and the
structure of the myocardium under varying conditions of adrenal
imbalance.

Method of Operation

The experiments were carried out with 70 male rats, with an
average weight of 160 g, divided into 4 groups: Group I -- reference
animals; Group II -- animals subjected to unilateral adrenalectomy;
Group III -- animals subjected to bilateral adrenalectomy (bilateral
adrenalectomy -- the adrenalectomy in the last two groups was carried
out at the same time, 7 days before the experiment); Group IV -- animals,
each of which, before being restrained, were administered 3 hydro-
cortisone injections in doses of 5 mg per 100 g of body weight.

* Numbers in the margin indicate pagination in the foreign text.

Each group included animals in the following experimental conditions, from which the following series were sacrificed: normal feeding (N); fasting and thirsting for 44 hours (F + S); fasting, thirsting and restraint for 24 hours (I), at 72 hours before the start of the experiment (72 h). The mortality rate was followed up and the glycemia was determined by the Hagedorn Jensen method; in the urine 17-CS (Zimmermann method), 17-OH (Porter Zilber method), Na and K ions (Lundegardh and Lehnekhnecht method), P (Brigge method), Mg (Kolhof method) were analytically determined; in addition, electrocardiographic studies were made (with the Cardior apparatus), morphological (hematoxylin eosin dying according to van Giessen and Simionescu) and histochemical examinations (using the Lie and Nielsen Selye technique for fuchsinophilics, the PAS method for mucopolysaccharides, the Hotchkiss-McManus method for glycogen) were carried out for studying the myocardium and the adrenal glands, using also histo-enzymatic methods for the myocardium (the Nachlas method for SDH, the Gomori-Bitenschi technique for the acid phosphatase and the Wachtein and Meisel method for the ATP-ase).

Results

The highest increase in the mortality during the restraint was encountered in animals subjected to bilateral adrenalectomy (75%), which, as a matter of fact, was noted also after fasting (33%) (Fig. 2). The electrolyte eliminations exhibited similar variations in all of the experimental groups; however, it should be mentioned that the elimination of K, P and Mg was higher in animals with endocrine imbalance, in particular in those treated with hydrocortisone (Fig. 1). The glycemia decreased in the reference animals and in those subjected to unilateral adrenalectomy after fasting and restraint, while it was at a high level in animals subjected to bilateral adrenalectomy and in those treated with hydrocortisone (Fig. 2). The 17-CS eliminations decreased after adrenalectomy, and after fasting it obviously increased in these animals (Fig. 2); after

restraint in the reference animals and in those treated with hydrocortisone the values decrease at the same proportion, growing 72 hours after the restraint was applied. The 17-OH elimination was not affected after endocrine imbalance; however, fasting favored the highest increase of the elimination in animals treated with hydrocortisone; after restraint, the values among the groups were identical.

The electrocardiographic examination of animals with adrenal imbalance revealed repolarizing modifications, in the sense of the decrease of the amplitude of the T waves. After fasting, we observed a micro-voltage in all of the animals; this was especially marked in animals subjected to bilateral adrenalectomy. The restraint induced similar changes of the rhythm between the groups, with certain minor differences. Thus, we encountered changes of the rhythm (the frequency decreased from 250 to 150 beats/minute) of the behavior (grade I A-V blockage, intraventricular blockage), of the terminal phase (wide S waves, uneven ST segments); the repolarization was fast, with positive, sharp and symmetrical T waves, which in rare cases were negative; in most of the animals, a U wave was present. In a small number of animals treated with hydrocortisone we encountered atrial fibrillations or tachycardia.

Microscopic examination of the myocardium after fasting revealed protein dystrophy and fuchsinophilic reaction of the myocardial fiber (Fig. 3) in all of the groups, localized in the subepicardial zone in the reference groups and distributed throughout the whole surface in the other groups. Edema and plasmorrhagia were more evident in the group which was administered hydrocortisone. The glycogen content was often low. Associated restraint increased the zones of micronecrosis in all the groups, and in the animals with adrenal imbalance the striations of the myocardial fibers disappear; in many zones the fuchsinophilic character was found to be intense, the edema and plasmorrhagia were obvious (Fig. 4). In the animals treated

with hydrocortisone the lesions affect also the supports. Microscopic examination of the adrenal glands in animals subjected to unilateral adrenalectomy and in the reference animals revealed, after fasting, hypertrophy with hyperplasia of the fasciculate zone and a nonhomogeneous repartition of the lipids, while in the animals treated with hydrocortisone a massive loading with lipids was observed (Fig. 5). After restraint, in the animals treated with hydrocortisone in the fasciculate zone a lipid depletion is encountered, while in the animals with unilateral adrenalectomy the cells were transformed into vacuolated spongiocytes (Fig. 6) and the lipid content increased. The medulla was intensively congestive (Fig. 7).

72 hours after the restraint, the microscopic and electrocardiographic aspects observed during the time of restraint persisted in the animals subjected to unilateral adrenalectomy.

Discussion

The relative similarity of the biochemical, electrocardiographic and morphological data observed after fasting or restraint between the groups subjected to adrenalectomy and the reference animals is attributed to the fact that the male rats which have subsidiary adrenals [3, 6, 9] were used in the experiments. However, the reduced capacity of these supernumerary glands to substitute for the functions of the adrenal glands caused perturbations in various metabolic processes, lowering the resistance of the organism (increased mortality) and affecting the power of adaptability with respect to a stressing agent. Activation of these subsidiary adrenal cells is not sufficient to satisfy the demands of the organism in glucocorticoids at the time of an attack when there is an excess of catecholamines from the extra-adrenal deposits. This probably causes the reduction of the energy metabolism, the increase of the permeability of the lysosome membrane with cytoplasmatic lysis through the action of proteolytic enzymes, thus structural modifications, which, together

with the ionic imbalance which determines the decrease of the potassium gradient, change the electrical activity of the myocardium.

We attribute the higher resistance observed in animals subjected to unilateral adrenalectomy to a better adaptability to new conditions in comparison with animals with bilateral adrenalectomy, which would explain the importance of certain values of the adrenal hormones /91 with respect to normal or unusual but more intensive stresses.

The fact that in the microscopic examination of the myocardium we found multiple pathologic elements, in comparison with the reference animals, in the animals subjected to unilateral adrenalectomy, leads us to state that the pathological modifications during the restraint are favored more by the excess of catecholamines and less by the endogenous corticoids. If by exogenous administration a certain corticoid dose is exceeded, it could be transformed into a noxious factor for the heart, blocking pyruvate oxidation, reducing the ATP synthesis, causing an enzyme insufficiency which could be followed by an ionic imbalance. Swingle et al. (cited by [6]) believe that the glucocorticoids could both improve or aggravate the overall state of the organism, just as we observed it in our own studies. E. Bajusz [1] showed that an excess of adaptive hormones could, under certain circumstances, cause disturbances or condition their generation.

Conclusions

In view of the investigation described in this communication, we may assume that facing a stressing action which determines a true disturbance of the homeostasis of the organism, both the excess and the reduction of adrenal hormones may favor the production of myocardial lesions and the reduction of the general resistance of the organism.

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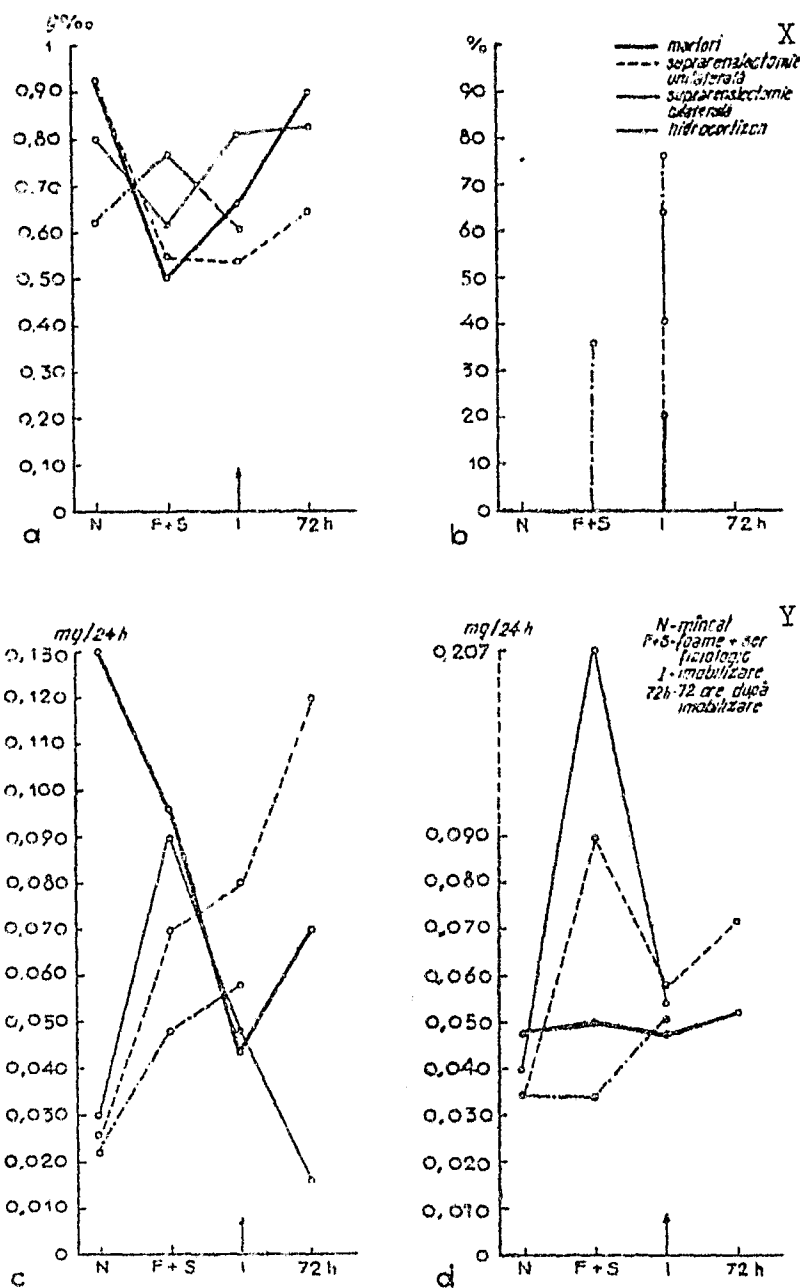


Figure 2. Average values of glycemia (a), urinary elimination of 17-CS (c), 17-OH (d) and the mortality expressed in percentages (b) in male rats subjected to restraint on a background of adrenal imbalance.

Key: X — reference animals
 ----- unilateral adrenalectomy
 bilateral adrenalectomy
 - . - . - hydrocortisone

Y N: fed
 F + S: physiological thirsting and fasting
 I: restraint, 72h -- 72 hours after restraint

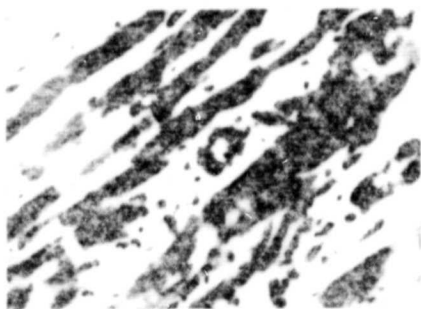


Figure 3. Myocardium
-- protein dystrophy,
fuchsinophilic reaction

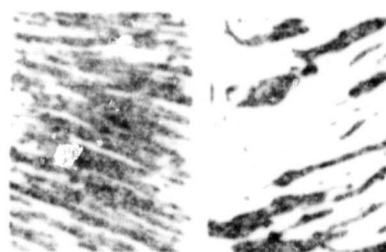


Figure 4. Myocardium
-- zone of micronecroses,
plasmorrhagia

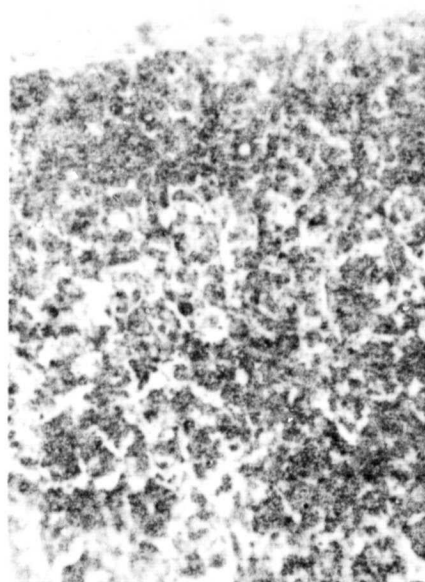


Figure 5. Adrenal gland
-- loading with lipids in
the cortical zone

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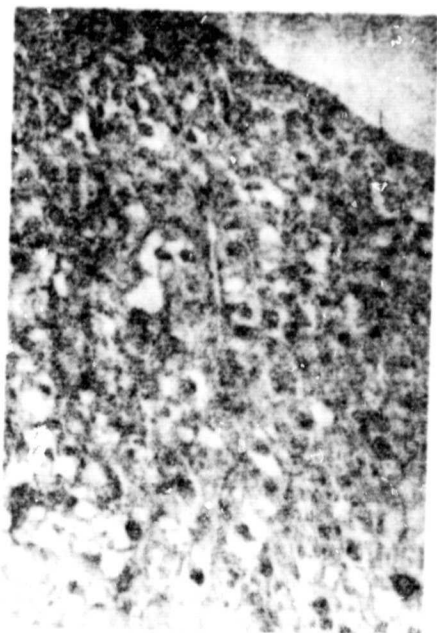


Figure 6. Adrenal gland -- spongiocyte aspect

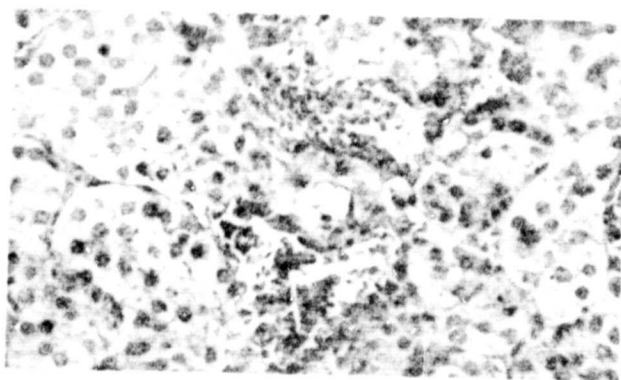


Figure 7. Adrenal gland -- medullar congestion